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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,413	06/23/2003	Denis Schrier	PCA391-D1-01-CFP	9188

28880 7590 07/11/2006

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EXAMINER	
OLSON, ERIC	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 07/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/602,413	SCHRIER ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,58 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 3, 58, and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted June 29, 2006 wherein claim 1 is cancelled, claims 2 and 58 are amended, and the specification is amended. This application is a divisional application of application 09/952787, now US patent 6620829, filed September 14, 2001, which claims benefit of provisional application 60/241119, filed October 17, 2000.

Claims 2, 3, 58, and 59 are pending in this application.

Claims 2, 3, 58, and 59 as amended are examined on the merits herein.

Applicant's amendments filed June 29, 2006 with respect to minor informalities in the title, specification and claim 2, of record stated in the Office Action dated March 28, 2006, have been fully considered and found to be persuasive to remove the objection as all the issues raised in these objections have been adequately addressed by the amendments. Therefore, said objections are withdrawn.

Applicant's amendment filed June 29, 2006 with respect to the rejection of claims 1-3, 58, and 59 made under 35 USC 112 second paragraph for an indefinite claim to a method of treatment without specifying a subject to be treated, of record stated in the Office Action dated March 28, 2006, has been fully considered and found persuasive to remove the rejection since a specific subject (i.e. a mammal) is identified in the claims as presently amended. Therefore, said rejection is withdrawn.

Applicant's amendment filed June 29, 2006 with respect to the rejection of claim 1 made under 35 USC 112 first paragraph for scope of enablement, for lacking enablement for a method of treating cartilage damage by administering a GABA analog of a formula other than formula I, of record stated in the Office Action dated March 28, 2006, has been fully considered and found persuasive to remove the rejection since claim 1 is no longer pending in this application. Therefore, said rejection is withdrawn.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lu et. al. (Included in PTO-1449 submitted by Applicant) in view of Minor (Editorial in *Arthritis & Rheumatism* (1996) v.9 iss.2 pp79-81) and the entry for Osteoarthritis in the Merck Manual, seventeenth edition (pp.449-451) (both references included in PTO-892 of record in the previous office action dated March 28, 2006).

Lu et. al. teach the use of gabapentin for the relief of nociceptive pain, including arthritic pain in particular. The data presented in figure 2, p. 217, demonstrate that administration of gabapentin to a rat suffering from experimentally induced arthritic pain reduces the severity of pain and hyperalgesia observed in the subject. The effect taught by this study is due to the relief of pain rather than the relief of inflammation, as

the extent of inflammation of the treated animal's paw was not observed to be any different from the control group. Lu et. al. do not teach the use of gabapentin for the treatment of noninflammatory cartilage damage in a mammal.

Minor teaches that regular exercise improves physical health, joint function, and muscle strength in patients suffering form osteoarthritis (OA). The Merck Manual (p. 451) teaches that, "Exercise (...) maintains healthy cartilage and range of motion and develops stress-absorbing tendons and muscles. Daily stretching exercises are of utmost importance. Immobilization for relatively short periods can accelerate or worsen the clinical course. Arrest and occasionally reversal of hip and knee OA can occur using well-planned exercise as therapy." It is also well known in the art that cartilage damage from OA can lead to pain which discourages patients from engaging in appropriate physical activity, leading to joint immobilization, muscle weakness, and weight gain, all of which accelerate the degeneration of the articular cartilage.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teaching of Lu et. al. by administering gabapentin to osteoarthritic patients who suffered from severe chronic pain which precluded them from engaging in a healthy level of physical activity. One would have been motivated to administer gabapentin to these patients both to improve their quality of life and to allow them to engage in therapeutic exercises and other physical activity which would partially prevent, block, or inhibit the course of the disease. One would have reasonably expected success in view of the well-established history of treating osteoarthritis with pain relieving medications. Although this line of reasoning does not involve a method of

treatment involving any direct inhibition of cartilage damage by gabapentin, it falls within the limits of the claimed invention. Specifically, the claims and specification fail to define the mechanism of action of the claimed method of treatment, or even to define that the claimed treatment must directly treat cartilage damage as opposed to indirectly treating it in the manner described. Accordingly, the invention taken as a whole is *prima facie* obvious.

Applicant's arguments submitted June 29, 2006 have been fully considered and have not been found to be persuasive to overcome the rejection of instant claims 2 and 3 under 35 USC 103.

Applicant asserts that there was no reasonable expectation of success for using gabapentin to treat noninflammatory cartilage damage at the time the present application was filed. However, Lu et al., in combination with Minor and Merck, demonstrate that there existed at the time of filing a reasonable expectation of success for a therapeutic regimen **comprising** administration of gabapentin to a mammal, as claimed by instant claims 2-3 and described by Lu et al. (p. 215, right column, fourth and fifth paragraphs), and **further comprising** appropriate exercise as described by Minor and Merck. Merck explicitly states that, "**Exercise (range or motion, isometric, isotonic, isokinetic, postural, strengthening) maintains healthy cartilage** and range of motion and develops stress-absorbing tendons and muscles." (p. 451, left column, second paragraph, cited above) This reference clearly teaches that the amount of cartilage lost in a patient who engages in regular exercise will be less than what would be lost by the same patient if the affected joint were kept immobile and not subjected to

exercise. It would have been obvious to one of ordinary skill in the art at the time of the invention that chronic pain in a joint would discourage a patient suffering from arthritis to exercise that joint, and thus to worsen the course of the disease and the degeneration of joint cartilage compared to if the patient had engaged in appropriate exercise. Thus in view of Lu et al. it would have been obvious that administering an analgesic such as gabapentin would increase the likelihood of the patient appropriately exercising the joint. The absence of specific data defining the exact benefit derived from specific types of exercise is not necessary for a finding of obviousness as the instant claims encompass all therapeutic regimens for the treatment of cartilage damage which involve as one step, either alone or in combination with any other conceivable step, administering gabapentin to a mammal. Thus there existed a reasonable expectation of success for administering gabapentin to a mammal as one step of a therapeutic method for the treatment of osteoarthritis.

Applicant further asserts that their invention omits the step of well-planned exercise while retaining its function of treating cartilage damage. However, the open-ended language of instant claims 2-3, "**comprising** administering to the mammal a therapeutically effective amount of a GABA analog," does not exclude such courses of therapy which comprise administration of gabapentin to a mammal and further comprise well-planned exercise. Said claims do not define a particular method of action by which the gabapentin exerts its effect. Nowhere in Applicant's disclosure is it demonstrated that gabapentin possess any activity other than its well-documented anticonvulsant and analgesic activities. Nowhere is it stated that the claimed cartilage-preserving effect is

exerted by a specific biochemical pathway unrelated to analgesia and the promotion of appropriate exercise. Applicant's specification (p. 207, lines 3-4) states that, regarding the EOA-rabbit experimental model, "the wounds were closed and the animals were housed in individual cages, **exercised**, and fed ad libitum." It is not disclosed whether all animals took advantage of the opportunity for exercise. While this model demonstrates that animals administered gabapentin displayed a reduced amount of cartilage damage, it fails to control for the amount of physical activity performed by treated vs. untreated rabbits. One reasonable interpretation of these data is that untreated rabbits remained immobile, due to joint pain, thus accelerating the clinical course of their condition, while treated rabbits were more physically active during the scheduled periods of exercise, thus maintaining healthier joints and slowing the rate of cartilage damage. The MIA rat model of osteoarthritis also fails to control for differing levels of physical activity. In contrast to other studies of potentially chondroprotective compounds, Applicant's disclosure does not include *in vitro* models of cartilage damage, such as bovine nasal cartilage cultures, which would measure chondroprotective effects directly without interference from confounding variables such as differing levels of physical activity.

Furthermore, the exercise-permitting pathway of cartilage preservation by gabapentin does not in every case require the deliberate introduction of exercise planned specifically for the purpose of treating cartilage damage. Within the claimed patient population of mammals in need of treatment for cartilage damage, there exists a subset of individuals whose regular lifestyle includes exercise, either planned as part of

a fitness program or as part of their normal level of physical activity. The mere step of administering an appropriate analgesic to these individuals would cause them to continue or resume their normal physical activity without hindrance from their arthritic condition, thus effectively treating their cartilage damage and slowing the degeneration of the cartilage in the effective joint. As noted above, it is reasonable to interpret Applicant's own animal experiments as having functioned in this manner.

Thus Applicants arguments are not found convincing and this rejection is made **FINAL**.

Claim Rejections – 35 USC § 101 Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 58 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 4 of prior U.S. Patent No. 6620829. Claim 59 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 5 of prior U.S. Patent No. 6620829.

Applicant's arguments submitted June 29, 2006 have been fully considered and have not been found to be persuasive to overcome the rejection of instant claims 58 and 59 under 35 USC 101. Claims 1, 4, and 5 of US 6620829 read as follows:

1. **A method** of treating noninflammatory cartilage damage in a mammal suffering therefrom, comprising administering a therapeutically effective amount of a GABA analog having the characteristic of being an inhibitor of cartilage damage, wherein the GABA analog is a compound of [formula III-IIIH]

4. **A method according to claim 1,** wherein the GABA analog is a compound named 3-(1-aminomethyl-cyclohexlymethyl)-4H-[1,2,4]oxadiazol-5-one, or a pharmaceutically acceptable salt thereof.

5. **A method according to claim 1,** wherein the GABA analog is a compound named 3-(1-aminomethyl-cyclohexlymethyl)-4H-[1,2,4]oxadiazol-5-one hydrochloride.

These claims are drawn to **methods of treating noninflammatory cartilage damage**, not compounds as asserted by Applicant. Therefore claims 4 and 5 of US 6620829 claim the exact same invention as instant claims 58 and 59. This rejection is therefore made **FINAL**.

Summary

No claims are allowed in this application. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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